

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization International Bureau



(43) International Publication Date
11 August 2005 (11.08.2005)

PCT

(10) International Publication Number
WO 2005/072087 A2

WO 2005/072087 A2

(51) International Patent Classification: Not classified (81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AI, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(21) International Application Number: PCT/US2004/041380

(22) International Filing Date: 10 December 2004 (10.12.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

| | | |
|------------|-------------------------------|----|
| 60/529,331 | 12 December 2003 (12.12.2003) | US |
| 10/847,087 | 17 May 2004 (17.05.2004) | US |
| 10/847,484 | 17 May 2004 (17.05.2004) | US |
| 60/625,707 | 5 November 2004 (05.11.2004) | US |

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Declaration under Rule 4.17:
— of inventorship (Rule 4.17(iv)) for US only

Published:

— without international search report and to be republished upon receipt of that report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: SYSTEM AND METHODS FOR NUCLEIC ACID AND POLYPEPTIDE SELECTION

(57) Abstract: This invention relates generally to systems and methods for identifying and selecting, desired proteins or nucleic acid molecules by linking mRNA, with known or unknown sequences, to its translated protein to form a cognate pair. The cognate pair is selected based upon desired properties of the protein or the nucleic acid. This method also includes the evolution of a desired protein or nucleic acid molecule by amplifying the nucleic acid portion of the selected cognate pair, introducing variation into the nucleic acid, translating the nucleic acid, attaching the nucleic acid to its protein to form a second cognate pair, and re-selecting this cognate pair based upon desired properties. Modified mRNAs operable to crosslink to tRNAs are also provided. Methods of producing a psoralen monoadduct or a crosslink are also provided. Methods of producing mRNA libraries and vaccines are also provided.

PATENT COOPERATION TREATY

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INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44bis)

| | | |
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| Applicant's or agent's file reference PRONOV.001BP | FOR FURTHER ACTION | See item 4 below |
| International application No. PCT/US2004/041380 | International filing date (<i>day/month/year</i>) 10 December 2004 (10.12.2004) | Priority date (<i>day/month/year</i>) 12 December 2003 (12.12.2003) |
| International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237 | | |
| Applicant PROTEONOA, INC. | | |

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|---|---|-------------------------------|--------------------------|---------------------|--------------------------|--|--------------------------|---------------------------------------|-------------------------------------|---|--------------------------|------------------------------------|--------------------------|--|--------------------------|--|
| <p>1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 bis.1(a).</p> <p>2. This REPORT consists of a total of 4 sheets, including this cover sheet.</p> <p>In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.</p> | | | | | | | | | | | | | | | | |
| <p>3. This report contains indications relating to the following items:</p> <table style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 15%; text-align: center; padding: 5px;"><input checked="" type="checkbox"/></td> <td style="width: 85%; text-align: left; padding: 5px;">Box No. I Basis of the report</td> </tr> <tr> <td style="text-align: center; padding: 5px;"><input type="checkbox"/></td> <td style="width: 85%; text-align: left; padding: 5px;">Box No. II Priority</td> </tr> <tr> <td style="text-align: center; padding: 5px;"><input type="checkbox"/></td> <td style="width: 85%; text-align: left; padding: 5px;">Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</td> </tr> <tr> <td style="text-align: center; padding: 5px;"><input type="checkbox"/></td> <td style="width: 85%; text-align: left; padding: 5px;">Box No. IV Lack of unity of invention</td> </tr> <tr> <td style="text-align: center; padding: 5px;"><input checked="" type="checkbox"/></td> <td style="width: 85%; text-align: left; padding: 5px;">Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</td> </tr> <tr> <td style="text-align: center; padding: 5px;"><input type="checkbox"/></td> <td style="width: 85%; text-align: left; padding: 5px;">Box No. VI Certain documents cited</td> </tr> <tr> <td style="text-align: center; padding: 5px;"><input type="checkbox"/></td> <td style="width: 85%; text-align: left; padding: 5px;">Box No. VII Certain defects in the international application</td> </tr> <tr> <td style="text-align: center; padding: 5px;"><input type="checkbox"/></td> <td style="width: 85%; text-align: left; padding: 5px;">Box No. VIII Certain observations on the international application</td> </tr> </table> <p>4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44bis.3(c) and 93bis.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44bis .2).</p> | <input checked="" type="checkbox"/> | Box No. I Basis of the report | <input type="checkbox"/> | Box No. II Priority | <input type="checkbox"/> | Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability | <input type="checkbox"/> | Box No. IV Lack of unity of invention | <input checked="" type="checkbox"/> | Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement | <input type="checkbox"/> | Box No. VI Certain documents cited | <input type="checkbox"/> | Box No. VII Certain defects in the international application | <input type="checkbox"/> | Box No. VIII Certain observations on the international application |
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| <input checked="" type="checkbox"/> | Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement | | | | | | | | | | | | | | | |
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| <p>The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland</p> <p>Facsimile No. +41 22 740 14 35</p> | <p>Date of issuance of this report 12 June 2006 (12.06.2006)</p> <p>Authorized officer Agnes Wittmann-Regis</p> <p>Telephone No. +41 22 338 89 70</p> |
|--|---|

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:
DANIEL E. ALTMAN
KNOBBE, MARTENS, OLSON AND BEAR, LLP
2040 MAIN STREET, FOURTEENTH FLOOR
IRVINE, CA 92614

REC'D 05 SEP 2005

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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

(PCT Rule 43bis.1)

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| Applicant's or agent's file reference PRONOVO.001BP | | Date of mailing (day/month/year) 01 SEP 2005 |
| International application No. PCT/US04/41380 | International filing date (day/month/year) 10 December 2004 (10.12.2004) | Priority date (day/month/year) 12 December 2003 (12.12.2003) |
| International Patent Classification (IPC) or both national classification and IPC IPC(7): C07H 21/04; C12Q 1/68 and US Cl.: 435/6; 536/23.1 | | |
| Applicant PROTEONNOVA, INC. | | |

1. This opinion contains indications relating to the following items:

| | | |
|-------------------------------------|--------------|--|
| <input checked="" type="checkbox"/> | Box No. I | Basis of the opinion |
| <input type="checkbox"/> | Box No. II | Priority |
| <input type="checkbox"/> | Box No. III | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability |
| <input type="checkbox"/> | Box No. IV | Lack of unity of invention |
| <input checked="" type="checkbox"/> | Box No. V | Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| <input type="checkbox"/> | Box No. VI | Certain documents cited |
| <input type="checkbox"/> | Box No. VII | Certain defects in the international application |
| <input type="checkbox"/> | Box No. VIII | Certain observations on the international application |

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

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| Name and mailing address of the ISA/ US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230 | Authorized officer Nancy T. Vogel Telephone No. (703) 308-0196 |
|--|--|

Form PCT/ISA/237 (cover sheet) (January 2004)

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/US04/41380

Box No. I Basis of this opinion

1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
 This opinion has been established on the basis of a translation from the original language into the following language _____, which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material
 a sequence listing
 table(s) related to the sequence listing
 - b. format of material
 in written format
 in computer readable form
 - c. time of filing/furnishing
 contained in international application as filed.
 filed together with the international application in computer readable form.
 furnished subsequently to this Authority for the purposes of search.
3. In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US04/41380

Box No. V Reasoned statement under Rule 43 bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N) Claims NON1-38 YES
Claims NONE NO

Inventive step (IS) **Claims** 1-38 **YES**
Claims NONE **NO**

Industrial applicability (IA) Claims 1-38 YES
Claims NONE NO

2. Citations and explanations:

Claims 1-38 meet the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest methods of evolving a protein sequence comprising linking mRNA molecule to its corresponding translated protein via a tRNA, wherein the mRNA is connected to said tRNA by a crosslinker, and wherein the mRNA comprises a crosslinker located on or near a stop codon.

Claims 1-38 the criteria set out in PCT Article 33(4), and thus have industrial applicability because the subject matter claimed can be made or used in industry.